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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/852,020	05/06/1997	ICHIRO MARUYAMA		6556

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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	38

DATE MAILED: 03/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	08/852,020	MARUYAMA ET AL.
	Examiner	Art Unit
	Gerald G Leffers Jr.	1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 27 November 2002.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 57-60 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 57-60 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The request for a continued prosecution application (CPA) under 37 CFR 1.53(d) filed on 7/12/02 is acknowledged. 37 CFR 1.53(d)(1) was amended to provide that the prior application of a CPA must be: (1) a utility or plant application that was filed under 35 U.S.C. 111(a) before May 29, 2000, (2) a design application, or (3) the national stage of an international application that was filed under 35 U.S.C. 363 before May 29, 2000. *See Changes to Application Examination and Provisional Application Practice*, interim rule, 65 *Fed. Reg.* 14865, 14872 (Mar. 20, 2000), 1233 *Off. Gaz. Pat. Office* 47, 52 (Apr. 11, 2000). A CPA for the instant invention was filed after May 29, 2000 (i.e. Paper No. 28 filed 7/5/01). Since a CPA of this application is not permitted under 37 CFR 1.53(d)(1), the improper request for a CPA is being treated as a request for continued examination of this application under 37 CFR 1.114. *See id.* at 14866, 1233 *Off. Gaz. Pat. Office* at 48.

As indicated in the Decision mailed to applicants on 1/31/03, a proper submission has been filed in the instant application as of 11/27/02. The submission filed on 11/27/02 as Paper No. 36 comprises an amendment of claims 57 and 59. Claims 57-60 are pending in the instant application.

Response to Amendment

The amendment filed in Paper No. 36 changes the scope of the claimed invention only marginally, if at all. The amendment changes the term "matrix anchor protein" to "head or tail protein", which appears to be nearly synonymous in scope to the original term. For this reason, the rejections of record are still applicable. Additional references are provided herein in support

of rejection of the pending claims under 35 U.S.C. 112 for lack of written description and for lack of enablement.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 57-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 57-60 encompass recombinant lambdoid bacteriophage vectors or bacteriophage having a cistron comprising the coding sequence for an anchor matrix gene operatively linked to coding sequences for a linker polypeptide and a desired, preselected polypeptide such that expression of the recombinant cistron during morphogenesis results in incorporation and display of the recombinant fusion polypeptide comprising the desired polypeptide sequence on the surface of the mature lambdoid phage particle. The claims encompass any of the head or tail polypeptides (e.g. head proteins: pE, pD, pW, pFII, pB*, pX1, pX2; tail proteins: pV, pJ, pG, pM and pT; page 22 lines 13-21), or portions thereof, as the matrix anchor component of the fusion polypeptide that is displayed on the surface of the phage particle. Each of these polypeptides has

its own unique structure and plays a unique role in phage morphogenesis, having a distinct set of temporal and spatial interactions with other phage proteins during the assembly of the mature phage particle. Thus, the instant claims are very broad genus claims directed to a number of distinct structural polypeptides having different structural and functional characteristics.

While the specification has described adequately one subset of the claimed genus, those embodiments drawn to the tail polypeptide pV, there is only the broadest description of any of the remaining members of the genus. The claims and specification only describe a conditionally expressible cistron encoding an anchor matrix polypeptide operatively linked to a linker polypeptide coding sequence which is in turn linked to the coding sequence for a desired, preselected polypeptide. There is no description of where within the coding sequence for any of the other members of the genus of potential anchor matrix polypeptides one would insert the sequences for the linker polypeptide and the desired polypeptide. There is no description in the prior art or within the specification as to which portions of any of the other anchor matrix polypeptides might be dispensable for morphogenesis and thus potentially suitable for insertion of foreign sequences. There are no relevant examples in the specification as filed of such a fusion construct for any of the potential anchor matrix polypeptides other than for pV. Because of the unique sequences, structural features and functions for each of the other anchor matrix proteins, one of skill in the art can not extrapolate from the description of fusion constructs comprising pV what would be a permissible insertion and fusion for any of the other anchor matrix proteins such that a recombinant polypeptide expressed from such a construct would be assembled and displayed on the surface of the mature phage particle.

The art teaches that the process of phage morphogenesis is exceedingly complex. Moody provides a post-filing review of phage assembly that describes how different types of phage have tackled the problem of encapsulating the phage genetic material in a protective structure that itself relies on a minimum of genetic information to encode the head structure (Michael F. Moody. Journal of Molecular Biology 1999, Vol. 293, pages 401-433; see the entire document). Generally speaking this involves using a minimum number of different protein subunits (i.e. requiring less genetic information) to form a complex 3-dimensional structure that can accommodate the genetic material (e.g. an icosahedron in the case of large dsDNA bacteriophage). To do this the major head protein subunits must be able to interact with one another in *equivalent* and *quasi-equivalent* ways that involve several protein-protein interactions for each subunit monomer. For example, the different head structures for different types of phage heads shown in Figure 3 each show how a single protein monomer (represented by the smaller triangles) can interact with itself to form axes of 5-fold or 6-fold symmetry within the same structure. Thus, at each vertex in the structures shown in Figure 3, each monomer of the major head protein can have a 5-fold or 6-fold interaction with adjacent proteins.

Moody teaches that as the required size of the phage head increases (i.e. to encapsulate a larger viral genome) additional proteins are required to help deal with an increased requirement for quasi-equivalent interactions amongst the subunits in assembly of the head structure. For example, these proteins would include endoscaffolding or exoscaffolding proteins and/or other proteins that can remain as part of the mature phage head (e.g. page 404, last paragraph of column 1 to column 2, second paragraph; page 407, column 1 to page 408, column 2). Moody teaches that assembly of the phage head is a complex process that is liable to errors, resulting in

malformed heads such as tubes, spirals or polyhedrons (e.g. page 408, column 2 to page 411, column 1). Moody further teaches that all of the larger dsDNA phage heads undergo some sort of maturation to form a more stable, stronger structure that is more resistant to mechanical or chemical stress and that results in a simultaneous increase in head volume (e.g. page 413, column 2 to page 416, column 1). This process involves modification of at least one of the phage head proteins such as proteolytic cleavage (e.g. T-even phage) or chemical modification (e.g. phage P22, lambda or T7). In the maturation process the protein-protein interactions of the subunits of the phage head are necessarily altered, even resulting in the translocation of subunit domains from the inner to the outer surface of the phage head (e.g. in phage T4) (page 414, columns 1-2). Thus, phage head assembly is a complex process, involving multiple protein-protein interactions that change during the process and involving several different types of proteins.

Given the great complexity of the claimed invention, wherein the fusion protein of the invention is displayed on the surface of the phage particle, as evidenced by the teachings of Moody, it would be helpful to be able to reliably predict the functional/structural characteristics of a given fusion protein based upon its primary sequence alone. Unfortunately, the art teaches that the relationship between the sequence of a protein and its tertiary structure (in essence the structure which defines its activity), is not well understood and is not predictable as evidenced by Berendsen (Science. 1998, Vol. 282, pages 642-643; see the entire document). This reference teaches that "Thus, one of the "grand challenges" of high-performance computer-predicting the structure of proteins-acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur: It is extremely desirable to possess but extremely elusive to obtain." (Page 643, columns 1-2). The whole reference teaches about the unpredictability in the art concerning

protein structure, and failures to make it predictable. Thus, as taught by Berendsen, it is likely that the first envisioned modification of a lambda phage head or tail protein to include a heterologous sequence would not be successful because one cannot predict a priori the final structure and functional characteristics of the fusion protein based upon primary sequence alone.

Given the broad genus of possible fusion proteins encompassed by the rejected claims and the lack of teachings in the instant specification or prior art that provide a basis for the skilled artisan to envision specific embodiments of the claimed invention, it would not have been possible for the skilled artisan to envision a representative number of the remaining members of the broadly claimed genus of recombinant anchor-matrix fusion proteins. Therefore, there is not sufficient description in the specification to inform a skilled artisan that the applicant was in possession of the full, large genus of recombinant phage embraced by the claimed invention: a recombinant lambdoid bacteriophage vector or bacteriophage comprising a cistron encoding an head or tail polypeptide other than pV operatively linked to the coding sequence for a linker polypeptide and desired, preselected polypeptide for display of the recombinant fusion protein on the surface of the mature phage.

Claims 57-60 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a recombinant lambdoid bacteriophage vector or bacteriophage comprising fusions with lambdoid bacteriophage tail polypeptides that are pV, does not reasonably provide enablement for embodiments wherein the lambdoid phage anchor matrix protein is other than pV. The specification does not enable any person skilled in the art to which

it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The nature of the invention is complex, involving a recombinant lambdoid bacteriophage which displays on the surface of the bacteriophage a fusion protein including one of the anchor matrix proteins operatively linked in the direction of the amino terminus to the carboxy terminus to a linker polypeptide and a polypeptide of choice. This invention further involves complex issues of which phage matrix polypeptides are suitable for forming such fusion proteins both in terms of accessible display on the outer surface of the phage and in the ability of the phage to assemble properly once the fusion protein is expressed during morphogenesis. Once a suitable matrix polypeptide has been identified, there are still complex issues as to where to insert the linker and preselected polypeptide into the desired matrix polypeptide such that assembly is not impaired and accessible display is maintained. Issues of what size and type of polypeptide will be tolerated and displayed in an accessible manner for each desired polypeptide are also present for the instant claims.

Assembly of the phage head is a complex process. Moody provides a post-filing review of phage assembly that describes how different types of phage have tackled the problem of encapsulating the phage genetic material in a protective structure that itself relies on a minimum

of genetic information to encode the head structure (Michael F. Moody. Journal of Molecular Biology 1999, Vol. 293, pages 401-433; see the entire document). Generally speaking this involves using a minimum number of different protein subunits (i.e. requiring less genetic information) to form a complex 3-dimensional structure that can accommodate the genetic material (e.g. an icosahedron in the case of large dsDNA bacteriophage). To do this the major head protein subunits must be able to interact with one another in *equivalent* and *quasi-equivalent* ways that involve several protein-protein interactions for each subunit monomer. For example, the different head structures for different types of phage heads shown in Figure 3 each show how a single protein monomer (represented by the smaller triangles) can interact with itself to form axes of 5-fold or 6-fold symmetry within the same structure. Thus, at each vertex in the structures shown in Figure 3, each monomer of the major head protein can have a 5-fold or 6-fold interaction with adjacent proteins.

Moody teaches that as the required size of the phage head increases (i.e. to encapsulate a larger viral genome) additional proteins are required to help deal with an increased requirement for quasi-equivalent interactions amongst the subunits in assembly of the head structure. For example, these proteins would include endoscaffolding or exoscaffolding proteins and/or other proteins that can remain as part of the mature phage head (e.g. page 404, last paragraph of column 1 to column 2, second paragraph; page 407, column 1 to page 408, column 2). Moody teaches that assembly of the phage head is a complex process that is liable to errors, resulting in malformed heads such as tubes, spirals or polyhedrons (e.g. page 408, column 2 to page 411, column 1). Moody further teaches that all of the larger dsDNA phage heads undergo some sort of maturation to form a more stable, stronger structure that is more resistant to mechanical or

chemical stress and that results in a simultaneous increase in head volume (e.g. page 413, column 2 to page 416, column 1). This process involves modification of at least one of the phage head proteins such as proteolytic cleavage (e.g. T-even phage) or chemical modification (e.g. phage P22, lambda or T7). In the maturation process the protein-protein interactions of the subunits of the phage head are necessarily altered, even resulting in the translocation of subunit domains from the inner to the outer surface of the phage head (e.g. in phage T4) (page 414, columns 1-2). Thus, phage head assembly is a complex process, involving multiple protein-protein interactions that change during the process and involving several different types of proteins.

Breadth of the claims: The breadth of the claims, encompassing any of the proteins displayed on the surface of the phage particle (e.g. head proteins: pE, pD, pW, pFII, pB*, pX1, pX2; tail proteins: pV, pJ, pG, pM and pT; page 22 lines 13-21), greatly increases the complexity of the invention with regard to how each potential matrix anchor protein is assembled into the phage, the role each potential matrix anchor protein plays in morphogenesis and assembly (i.e. is it dispensable for proper assembly and function?) and where within the coding region for the potential matrix anchor protein to insert the coding sequences for the polypeptide linker and preselected polypeptide in order to express a fusion protein that will allow its incorporation into the phage capsid in such a way as to allow morphogenesis and accessible display of the preselected protein on the mature phage particle.

Guidance of the specification/The existence of working examples: The specification provides specific guidance and working examples only for the major tail protein pV and the prior art is silent on fusion proteins that include the other tail proteins or head proteins of lambdoid phage. Reference to the other outer-surface proteins of the phage particle is only suggestive that

they are suitable for use in the invention by virtue of their location on the surface of the phage tail and capsid. There is no guidance within the specification as filed regarding which portions of the other potential matrix anchor proteins are dispensable for assembly and which may present suitable locations for insertion of heterologous sequences. There is no guidance within the specification as filed as to which particular nucleotide sequences within the gene encoding any potential matrix anchor protein, other than pV, is suitable for insertion of a heterologous coding sequence such that the expressed fusion protein from such a construct will not disrupt particle assembly and will allow functional, accessible display of the desired preselected polypeptide on the mature phage particle.

State of the art: The state of the art at the time of applicants' invention was high, requiring a high degree of skill in order to make and use the claimed invention. In fact, there is no guidance in the prior art regarding which portions of the potential matrix anchor proteins are dispensable for assembly and which may present suitable locations for insertion of heterologous sequences. There is no guidance within the prior art as to which particular nucleotide sequences within the gene encoding any potential matrix anchor protein are suitable for insertion of a heterologous coding sequence such that the expressed fusion protein from such a construct will not disrupt particle assembly and will allow functional, accessible display of the desired preselected polypeptide on the mature phage particle.

Predictability of the art: In general, the art of predicting how a particular protein will fold to form the structure which provides its functionality is not exact. This is because the relationship between the sequence of a protein and its tertiary structure (in essence the structure which defines its activity), is not well understood and is not predictable as evidenced by

Berendsen (Science. 1998, Vol. 282, pages 642-643; see the entire document). This reference teaches that "Thus, one of the "grand challenges" of high-performance computer-predicting the structure of proteins-acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur: It is extremely desirable to possess but extremely elusive to obtain." (Page 643, columns 1-2). The whole reference teaches about the unpredictability in the art concerning protein structure, and failures to make it predictable. Thus, as taught by Berendsen, it is likely that the first envisioned modification of a lambda phage head or tail protein to include a heterologous sequence would not be successful because one cannot predict a priori the final structure and functional characteristics of the fusion protein based upon primary sequence alone.

That the art of displaying a desired fusion polypeptide in an accessible manner on a phage particle is not predictable, as evidenced by applicants' own teachings. The specification discloses that the pV is present in 180-200 copies in the mature tail. The specification teaches (page 115, 1st paragraph) that addition of a linker polypeptide appears to interfere with tail assemble, since the plaques were smaller in su^+ hosts. Further, at page 126 of the specification it is disclosed that phage tails displaying beta-galactosidase contained only one to a few copies of the fusion polypeptide even though higher levels of incorporation could have been expected, indicating the fusion polypeptide interferes with some aspect of tail assembly or infection. Therefore, successful incorporation into a mature tail of pV protein fusions is somewhat unpredictable.

Each of the matrix proteins occupies a unique position in the mature particle, and performs a unique role during particle assembly. The successful incorporation into the tail of altered forms of one of the tail proteins (e.g. pV) does not provide evidence that any of the other

matrix proteins (head or tail proteins) can be similarly modified without impairing their unique role in phage assembly. With respect to the pV protein, it was known in the prior art that this protein comprised a "knob" that extended out from the surface of the phage that was dispensable. It is this "knob" that is replaced by the displayed peptide in the disclosed invention. Replacement of this "knob" with a heterologous peptide sequence would not have been expected *a priori* to interfere with phage assembly. However, as disclosed in the instant specification it was necessary to replace the knob with the desired peptide in only a limited number of recombinant pV subunits in the phage tail, or assembly was impaired. It is for this reason that Ladner is not deemed to be prior art for the prophetic disclosure of using pV peptide fusions to display proteins. No comparable dispensable peptide sequence is disclosed in either the specification or prior art that one could have expected could be replaced with a desired peptide, without interfering with phage assembly. As recited in the claims, the fusion polypeptide comprises, from amino to carboxy terminus, a matrix anchor polypeptide, a linker polypeptide and a preselected polypeptide. Such an arrangement would therefore require that the carboxy terminus of a given matrix anchor protein be exposed on the surface of the particle and that the addition of other polypeptides to the carboxy terminus of the matrix anchor polypeptide not interfere with either expression of the matrix anchor gene or assembly of the matrix anchor/preselected polypeptide fusion into the phage.

Applicants have submitted Mikawa et al (Exhibit 1, Paper No. 8) as evidence of enablement for other capsid or tail proteins. However, Mikawa et al is not prior art and it is not clear that the methods used to obtain phage displaying polypeptides as pD fusions are commensurate with the teachings of the instant disclosure. For example, amino terminal fusions

were made between the second and third codons, rather than at or after the initial codon (page 22, column 1). It is also noted that the primary author, Y.G. Mikawa, is not a named inventor on the instant application, which suggests that the contribution of Y.G. Mikawa is in addition to the instant disclosure. With regard to the predictability of making fusions comprising pD as the matrix anchor portion of the fusion polypeptide, it is of note that the reference states in the first paragraph of the discussion (page 27) that the ends of pD are not involved in the interaction between pD subunits or between pD and pE subunits, "...an important result for which no guarantee existed at the start of this work.". As indicated above, there is no teaching or working example in the instant specification that indicates where in the pD coding sequence (or in the coding sequence of any of the other potential matrix anchor proteins) it is appropriate to insert coding sequences for the linker polypeptide and the preselected protein such that interaction among capsid components is not interrupted, that phage assembly is not impaired and the desired fusion protein is displayed in a functional, accessible manner. Also, as with pV, one cannot extrapolate from pD fusions where to make fusions to other capsid proteins, such that phage assembly is not impaired. Mikawa et al specifically states that the authors chose pD because it was dispensable provided the genome was less than 82% of wild type in length, a feature not true for the other capsid proteins.

The amount of experimentation necessary: Given the complex nature of the invention in which a fusion polypeptide comprising an anchor motif from the bacteriophage matrix is expressed during phage morphogenesis such that the fusion polypeptide is incorporated into the phage structure and displayed in an accessible and/or functional manner, the breadth of the claims which encompass any of the potential matrix anchor polypeptides displayed on the

surface of the phage particle, the lack of guidance from the specification or the prior art as to which portions of any of the other potential matrix anchor proteins are dispensable for phage assembly or which would be appropriate for insertion of the coding sequences for the polypeptide linker and preselected polypeptide (even for pD) and the unpredictability of whether a particular fusion will be incorporated into the phage particle in a fashion that does not disrupt subunit-subunit interaction and will allow accessible and/or functional display of the desired, preselected polypeptide on the mature particle, it would require undue, unpredictable experimentation to make even one embodiment of the claimed invention not involving pV as the matrix anchor protein. One would first have to envision an appropriate matrix anchor protein construct in which the coding sequence for the matrix anchor protein is operatively linked at a particular sequence with the coding sequences for a linker polypeptide and desired, preselected polypeptide, make the construct and express the hybrid gene during morphogenesis such that the fusion protein might be incorporated into the phage particle and then determine whether functional phage particles are formed which display the desired, preselected polypeptide sequence in an accessible and/or functional manner. If unsuccessful, which is likely given the lack of guidance from the specification or the prior art as to which portions of the other potential matrix anchor proteins are dispensable for particle assembly and the unpredictability of the art as evidenced by applicants' own teaching regarding pV, it would then be necessary for one of skill in the art to envision a modification of the first matrix anchor/fusion protein construct, or an entirely different construct, which might be suitable for display of a desired protein on the surface of the phage particle, make the construct and express the hybrid gene during morphogenesis such that the second fusion protein might be incorporated into the phage particle

and then determine whether functional phage particles are formed which display the desired, preselected polypeptide sequence in an accessible and/or functional manner. If again unsuccessful, which is likely given the lack of guidance from the specification or the prior art as to which portions of the other potential matrix anchor proteins are dispensable for particle assembly and the unpredictable nature of the art as evidenced by applicants' own teachings regarding pV, it would be necessary for one of skill in the art to repeat the entire process until such time, if any, that a construct was identified which allows the expression of a fusion protein comprising one of the potential matrix anchor proteins with a desired, preselected polypeptide such that the fusion protein is successfully incorporated into the mature phage particle and the preselected polypeptide displayed in an accessible and/or functional manner. Such experimentation is undue, unpredictable experimentation and would be required in order to make and use any embodiment of the instant invention not comprising pV as the matrix anchor portion of the fusion protein, even the pD fusions of Mikawa et al, in light of the instant specification. Thus, applicants' claimed invention of a recombinant lambdoid bacteriophage vector or bacteriophage encoding protein fusions derived from any matrix anchor protein located on the surface of the phage particle operatively linked to a polypeptide linker and preselected polypeptide, is not considered to be fully enabled by the specification. Only in the case where the matrix anchor protein is derived from the pV polypeptide, as described in the specification, would there be a reasonable expectation of success in constructing a vector or bacteriophage which encodes a fusion polypeptide comprising the desired, preselected polypeptide expressed and displayed in an accessible and/or functional manner.

Response to Arguments

Applicant's arguments filed on 11/27/03 have been fully considered but they are not persuasive. The response merely reiterates arguments that have been made previously in prosecution and which have been dealt with, for example, in Papers No. 20, 26 and 29.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

Ggl
March 10, 2003